AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A polypeptide having a binding affinity for HER2, wherein the sequence of the polypeptide comprises the sequence of a protein Z, as set forth in SEQ ID NO:1, having from 4 to about 20 substitution mutations thereon, comprising at least four substitution mutations at the positions 13, 14, 28, 32 and 35 of SEQ ID NO:1, wherein the mutations comprise at least three of the following substitution mutations:

(a) from phenylalanine to tyrosine at position 13 of SEQ ID NO:1,

(b) from tyrosine to tryptophan at position 14 of SEQ ID NO:1,

(c) from glutamine to arginine at position 32 of SEQ ID NO:1, and

(d) from lysine to tyrosine at position 35 of SEQ ID NO:1.

2. (Previously Presented) A polypeptide according to claim 1, which has a binding affinity for HER2 such that the K_D value of the interaction is at most 1×10^{-6} M.

3. (Previously Presented) A polypeptide according to claim 2, which has a binding affinity for HER2 such that the K_D value of the interaction is at most 1×10^{-7} M.

4. (Cancelled).

5. (Cancelled).

6. (Cancelled).

7. (Currently Amended) A polypeptide according to claim 1, additionally comprising substitution mutations at one or more of the positions 9, 10, 11, 17, 18, 24, 25 and 27 of SEQ ID NO:1.

8. (Cancelled).

9. (Cancelled).

10. (Currently Amended) A polypeptide according to claim 1, comprising a substitution mutation at position 28 of SEQ ID NO:1 from asparagine to an amino acid residue selected from arginine and histidine.

11. (Currently Amended) A polypeptide according to claim 1, comprising a substitution mutation at position 28 of SEQ ID NO:1 from asparagine to arginine.

12. (Cancelled).

13. (Cancelled).

14. (Currently Amended) A polypeptide according to claim 1, comprising a substitution mutation at position 10 of SEQ ID NO:1 from glutamine to arginine.

15. (Currently Amended) A polypeptide according to claim 1, comprising a substitution mutation at position 11 of SEQ ID NO:1 from asparagine to threonine.

16. (Currently Amended) A polypeptide according to claim 1, comprising a substitution mutation at position 17 of SEQ ID NO:1 from leucine to valine.

17. (Currently Amended) A polypeptide according to claim 1, comprising a substitution mutation at position 27 of SEQ ID NO:1 from arginine to an amino acid residue selected from lysine and serine.

18. (Currently Amended) A polypeptide according to claim 60, comprising at least the following mutations: F13Y, Y14W, N28R,

Q32R and K35Y, wherein the amino acid positions are relative to SEQ ID NO:1.

19. (Previously Presented) A polypeptide according to claim 1, the amino acid sequence of which is selected from the group consisting of SEQ ID NO: 2-4 and 6-79.

20. (Previously Presented) A polypeptide according to claim 19, the amino acid sequence of which is selected from the group consisting of SEQ ID NO:2-3.

21. (Previously Presented) A polypeptide according to claim 1, in which at least one of the asparagine residues present in the protein Z has been replaced with another amino acid residue.

22. (Currently Amended) A polypeptide according to claim 21, comprising substitution mutations at at least one position of SEQ ID NO:1 chosen from N3, N6, N11, N21, N23, N28, N43 and N52.

23. (Currently Amended) A polypeptide according to claim 22, comprising at least one of the following mutations of SEQ ID NO:1: N3A, N6A, N6D, N11S, N23T, N28A and N43E.

24. (Previously Presented) A polypeptide, which constitutes a fragment of a polypeptide according to claim 1, which fragment retains binding affinity for HER2.

25. (Previously Presented) A polypeptide according to claim 1, which comprises additional amino acid residues at either terminal.

26. (Previously Presented) A polypeptide according to claim 25, in which the additional amino acid residues comprise a cysteine residue at the N- or C-terminal of the polypeptide.

27. (Previously Presented) A polypeptide according to claim 25, in which the additional amino acid residues comprise a tag, preferably chosen from a hexahistidinyl tag, a myc tag and a flag tag.

28. (Currently Amended) A polypeptide according to claim 25, in which the additional amino acid residues comprise at least one functional polypeptide domain, so that the polypeptide is a fusion polypeptide between a first moiety, consisting of a polypeptide having a binding affinity for HER2, wherein the sequence of the polypeptide comprises the sequence of a protein

Z, as set forth in SEQ ID NO:1, having from 4 to about 20 substitution mutations thereon and comprising at least four substitution mutations at the positions 13, 14, 28, 32 and 35 of SEQ ID NO:1, and at least one further moiety.

29. (Currently Amended) A polypeptide according to claim 28, in which the further moiety consists of one or more polypeptide(s) having a binding affinity for HER2, wherein the sequence of the polypeptide comprises the sequence of a protein Z, as set forth in SEQ ID NO:1, having from 4 to about 20 substitution mutations thereon and comprising at least four substitution mutations at the positions 13, 14, 28, 32, and 35 of SEQ ID NO:1, making the polypeptide a multimer of HER2 binding polypeptides, the sequences of which may be the same or different.

30. (Previously Presented) A polypeptide according to claim 28, in which the further moiety comprises at least one polypeptide domain capable of binding to a target molecule other than HER2.

31. (Previously Presented) A polypeptide according to claim 30, in which the further moiety comprises at least one polypeptide domain capable of binding to human serum albumin.

32. (Previously Presented) A polypeptide according to claim 31, in which the at least one polypeptide domain capable of binding to human serum albumin is the albumin binding domain of streptococcal protein G.

33. (Previously Presented) A polypeptide according claim 30, in which the further moiety comprises a polypeptide wherein the sequence of the polypeptide comprises the sequence of a protein Z, as set forth in SEQ ID NO:1 having from 1 to about 20 substitution mutations.

34. (Cancelled).

35. (Previously Presented) A polypeptide according to claim 28, in which the further moiety is capable of enzymatic action.

36. (Previously Presented) A polypeptide according to claim 28, in which the further moiety is capable of fluorescent action.

37. (Previously Presented) A polypeptide according to claim 28, in which the further moiety is a phage coat protein.

38. (Previously Presented) A polypeptide according to claim 1, which further comprises a label group.

39. (Previously Presented) A polypeptide according to claim 38, in which the label group is selected from the group consisting of fluorescent labels, biotin and radioactive labels.

40. (Previously Presented) A polypeptide according to claim 1, coupled to a substance having an activity against cells overexpressing HER2.

41. (Previously Presented) A polypeptide according to claim 40, in which said substance having an activity against cells overexpressing HER2 is selected from the group consisting of cytotoxic agents, radioactive agents, enzymes for antibody-directed enzyme prodrug therapy applications (ADEPT), cytokines and procoagulant factors.

42. (Cancelled).

43. (Cancelled).

44. (Cancelled).

45. (Cancelled).

46. (Cancelled).

47. (Previously Presented) A method of treatment of at least one form of cancer characterized by overexpression of HER2, which method comprises administering to a subject in need of such treatment a therapeutically effective amount of a composition, which comprises a polypeptide according to claim 1 as an active substance.

48. (Cancelled).

49. (Previously Presented) A method of directing a substance having an anti-cancer activity to cells overexpressing HER2 *in vivo*, which method comprises administering a conjugate of said substance and a polypeptide according to claim 1 to a subject.

50. (Cancelled).

51. (Cancelled).

52. (Previously Presented) A method of detection of HER2 in a sample, comprising the steps: (i) providing a sample to be tested, (ii) applying a polypeptide according to claim 1 to the sample under conditions such that binding of the polypeptide to any HER2 present in the sample is enabled, (iii) removing non-bound polypeptide, and (iv) detecting bound polypeptide.

53. (Previously Presented) A method according to claim 52, in which the sample is a biological fluid sample, preferably a human blood plasma sample.

54. (Previously Presented) A method according to claim 52, in which the sample is a tissue sample.

55. (Cancelled).

56. (Previously Presented) A kit for *in vivo* diagnosis of HER2 overexpression, which kit comprises a polypeptide according to claim 1 labeled with a chelator, a diagnostic radioactive

isotope, and reagents for the analysis of the incorporation efficiency.

57. (Cancelled).

58. (Previously Presented) The method according to claim 54, wherein the sample is a human tissue sample.

59. (Previously Presented) The method according to claim 54, wherein the sample is a biopsy sample from a human suffering from cancer.

60. (Previously Presented) A polypeptide according to claim 1, comprising all the substitution mutations (a) - (d).